

## **ABSTRACT**

A process for constructing a catalogued nucleic acid library in which the proportional representation of the constituents is adjusted to advantage through the use of disclosed technologies for positive and negative selection. The resultant benefit is that significantly fewer library constituents will need to be screened in order to identify a potentially desired constituent. Moreover, library constituents that previously would have been essentially "lost" are now recoverable. Preferred embodiments of this invention include the cataloguing, normalization, and enrichment of library constituents. By way of example, but not limitation, this technology is serviceable for constructing a library that contains an adequate representation of desirable constituents that (1) are initially found in low-copy numbers within a sample source or (2) originate from an organism that is problematic to culture. Applicable uses of this invention include any library-screening endeavor previously hindered by logistical impediments.

By expanding previous logistical frontiers this invention allows for a novel generation of previously unattainable molecules - particularly molecules that are "unclonable" from conventional, unadjusted libraries - to now be detected, cloned, manipulated, expressed, studied, and used. By disclosing the construction and screening of high yielding nucleic acid libraries from mixed and uncultivated organisms, the instant technology eclipses former boundaries in the area of biological discovery and enables the full breadth of biological diversity to be accessed in the search for previously undiscovered genes and gene products. The benefits of the present invention are seen to extend to areas of diagnosis, medicine, agriculture, manufacturing, and academia.